PATENT COOPERATION TREAT .

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 21 July 2000 (21.07.00)	
International application No. PCT/US99/25653	**Applicant's or agent's file reference** 18048-11PC
International filing date (day/month/year) 02 November 1999 (02.11.99)	**Priority date** (day/month/year) 03 November 1998 (03.11.98)
Applicant HAYDOCK, Paul, V. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

02 June 2000 (02.06.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 18048-11PC	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/25653	International filing date *(day/month/year)* 02 NOVEMBER 1999	Priority date *(day/month/year)* 03 NOVEMBER 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant **SAIGENE CORPORATION**		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02 JUNE 2000	08 JANUARY 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Cynthia Wilder Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/25653

I. Basis of the rep rt

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-27 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 28-33 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages 1-2 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/25653

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-14,18-22, 26, 35-37, 41-47	YES
	Claims	15-17, 23-25, 27-34, 38-40	NO
Inventive Step (IS)	Claims	41-47	YES
	Claims	1-40	NO
Industrial Applicability (IA)	Claims	1-47	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 15-17, 23-25, 27-34, and 38-40 lack novelty under PCT Article 33(2) as being anticipated by Stavrianopoulos et al. 4,994,373 . Regarding claims 15-17, 23-25, 28-34 and 38-40, Stavrianopoulos et al. teach a method of detecting a target analyte in a test sample, the method comprising: contacting a sample with a solid support which comprises a capture reagent that binds to the target analyte, wherein the solid support is coated with a non-stick coating material prior to contacting the sample; contacting the solid support with a signal reagent which binds to the target analyte; and determining whether the sample contains the target analyte by detecting the presence of signal reagent immobilized on the solid support (col. 8, lines 10-56). The reference also teach wherein the non-stick coating is a silanizing agent consisting silane (col. 8, lines 23-27). Stavrianopoulos et al. teach wherein the method comprises several washing steps and wherein the solid support is glass. The reference also teaches wherein the capture reagent covalently attached to the solid support (col. 7, lines 37-43) comprise a tag, wherein the tag is biotin and the tag binder is avidin or streptavidin or an antibody that binds to biotin (col. 10, lines 25-52). The reference teaches wherein the target analyte comprise a polynucleotide and the capture reagent comprise an oligonucleotide which hybridizes to the polynucleotide wherein the polynucleotide is DNA (col. 7, lines 41-45). The reference also teaches wherein the signal reagent comprises a detectable label attached to an antibody which specifically binds to double stranded nucleic acid (col. 10, lines 35-52). Therefore the claimed invention of claims 15-17, 23-25, 27-34 and 38-40 are anticipated by the reference of Stavrianopoulos et al.

Claims 1-14, 18-22, 26 and 37 lack an inventive step under PCT Article 33(3) as being obvious over Schnipelsky et al. 5,229,297, in view of Douglas 5,556,748 S and Stavrianopoulos et al. 4,994,373, (Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12Q 1/68, G01N 33/53, C12P 19/34, C12N 5/00, G01N 33/566 and US Cl.: 435/6, 435/7.1, 435/7.5, 435/91.2, 435/402, 436/501, 935/77, 935/78

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
as applied to claims 15-17, 23-25, 27-34 and 38-40 above and further in view of Ness et al. (Nucleic Acids Research,. Regarding claims 1-14, 18-22, 26 and 37, Schnipelsky et al. teach method of reducing cross-contamination of an assay reagent solution, the method comprising contacting a solid support with a first reagent solution, removing the solid support from contact with the first reagent, contacting the solid support with a second reagent, removing the solid support and contacting the solid support with one or more intermediate reagents solution, wherein the intermediate solution is a wash solution (col. 10, lines 13-46). The reference further teaches wherein the solid support is a glass bead (col. 12, lines 39-43). Schnipelsky et al. further teach wherein the reagents are placed into containers (cuvettes) (col. 9, lines 63-66). Schnipelsky et al. also teach wherein the solid support comprise a captured reagent which is able to specifically bind to target analyte and a substrate which produces a detectable product when contact with an enzyme (col. 10, lines 19-30 and col. 12.lines 39-43). The method of Schnipelsky et al. differ from that of the claimed invention in that Schnipelsky et al. do not teach wherein the solid support is coated with a non-stick material, wherein the non-stick coating material is selected from the group consisting of silane, dimethylchlorosilane and Gel-Slick, prior to contacting the solid support with a first reagent. The reference also does not teach wherein a denaturant such as a chaotropic agent or a detergent is utilized as the first reagent. Douglas teaches a method of detecting a target analyte wherein the solid support is coated with a non-stick material consisting of silane ,a capture probe covalently attached on the support and a substrate which produces a detectable product when contacted with an enzyme linked to a signal reagent (col. 2, lines 23-37). Douglas also discloses wherein the solid support consist of wells (col. 2, line 29-30). Stavrianopoulos et al. also teach a method of detecting a target analyte in a sample, comprising pretreating a solid support with a non-stick material consisting of silane (col. 8, Example 1). The method of Douglas and Stavrianopoulos et al. differ from that of the claimed invention in that references do not teach wherein the method comprise a first reagent comprising a denaturant selected from the group consisting of a chaotropic agent or a detergent. Ness et al. teach a method of detecting an analyte in a sample comprising contacting the sample with a denaturant consisting of a chaotropic agent, sodium thiocyanate(page 5144, col. 1, lines 4-5, see also Abstract). It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teaching of Schnipelsky et al. with the teachings of Douglas and Ness because the skilled artisan would have been motivated to utilized a chaotropic agent as a first reagent with a reasonable expectation of success to lyse the cells or organism of interest, inhibit nucleases and proteases and provide adequate binding stringency without chemically altering the target analyte as taught by Ness et al. (page 5143, col. 1, second paragraph). The skilled artisan would have been motivated to coated the solid support with a non-stick material such as silane for the obvious benefit of preventing cross-contaminants from binding to the solid support, thus reducing cross-contamination.

Claims 35 and 36 lack an inventive step under PCT Article 33(3) as being obvious Stavrianopoulos et al. as applied to claims 1-34 and 37-40 above. Regarding claims 35 and 36, Stavrianopoulos et al. teach a method of detecting a target analyte in a test sample, the method comprising: contacting a sample with a solid support which comprises a capture reagent that binds to the target analyte, wherein the solid support is coated with a non-stick coating material prior to contacting the sample; contacting the solid support with a signal reagent which binds to the target analyte;. and determining whether the sample contains the target analyte by detecting the presence of signal reagent immobilized on the solid support wherein the target analyte is a polynucleotide(col. 8, lines 10-56). The reference does not expressly teach wherein the polynucleotide is amplified prior to contacting the sample with the capture reagent. However, it is well known in the art that method of amplification are routinely use to increase the sample size prior to analysis. Therefore, it would have been obvious to one of ordinary skill in the art to amplify the polynucleotide sample prior to contacting with the capture reagent for the obvious benefit of increasing the amount of starting material for analysis.

---------- NEW CITATIONS ----------
US 5,229,297 A (SCHNIPELSKY et al) 20 JULY 1993, see entire reference.

NESS et al. The Use of Oligodeoxynucleotide Probes in Chaotrope-based Hybridization Solution. Nucleic Acids Research. December 1991, Vol. 19, No. 19, pages 5143-5151, see entire reference.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/25653

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C12Q 1/68, G01N 33/53, C12P 19/34, C12N 5/00, G01N 33/566

US CL :Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 435/7.1, 435/7.5, 435/91.2, 435/402, 436/501, 935/77, 935/78

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,556,748 (DOUGLAS) 17 September 1996, se entire reference.	1-47
Y	US 4,018,734 (DUMOULIN) 19 April 1977, column 7, lines 6-18. see also "abstract".	1-47
Y	US 4,994,373 (STAVRIANOPOULOS et al.) 19 February 1991, See entire reference.	1-47
A,P	FALIPOU, S. etal. New use of cyanosilane coupling agent for direct binding of antibodies to Silica supports. Physicochemical characterization of molecularly bioengineered layers. Bioconjugate Chemistry. March 1999, Vol. 10, no.3, see pages 346-353.	1-47

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"B"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
07 JANUARY 2000	03 FEB 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Cynthia Wilder Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/25653

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

435/6, 435/7.1, 435/7.5, 435/91.2, 435/402, 436/501, 935/77, 935/78

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

WEST 1.2, East, Medline, Biosis, Scisearch, CAS Registry
search terms: solid, support, solid support, contamination, cross-contamination, sandwich hybridization, solid phase, immobilize, coated, non-stick, silanes, reagent, reduce, prevent, dimethylchlorosilane, immunoassay, denaturant, detergent, wells or plate, glass or magnetic, amplified, amplification, antibody, capture, urea, guanidine, polynucleotide, label, dipstick, prong